Models and Languages for Computational Systems Biology

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School of Informatics
The University of Edinburgh

MLCSB runs in Semester 2, starting January 2010

Vital Statistics

Timing: MLCSB runs during Semester 2, starting January 2009

Lecturer: Ian Stark

Bioinformatics, Systems & Synthetic Biology

Computational Systems Biology (Semester 2)
Synthetic Biology: Modelling (Semester 1)

Theoretical Computer Science

Communication and Concurrency (Semester 1)
Performance Modelling (Semester 1)

Course web page: http://www.inf.ed.ac.uk/teaching/courses/mlcsb/

Systems Biology

Biology is the study of living organisms; Systems Biology is the study of the dynamic processes that take place within those organisms.

In particular:

- Interaction between processes;
- Behaviour emerging from such interaction; and
- Integration of component behaviours.

Systems Biology

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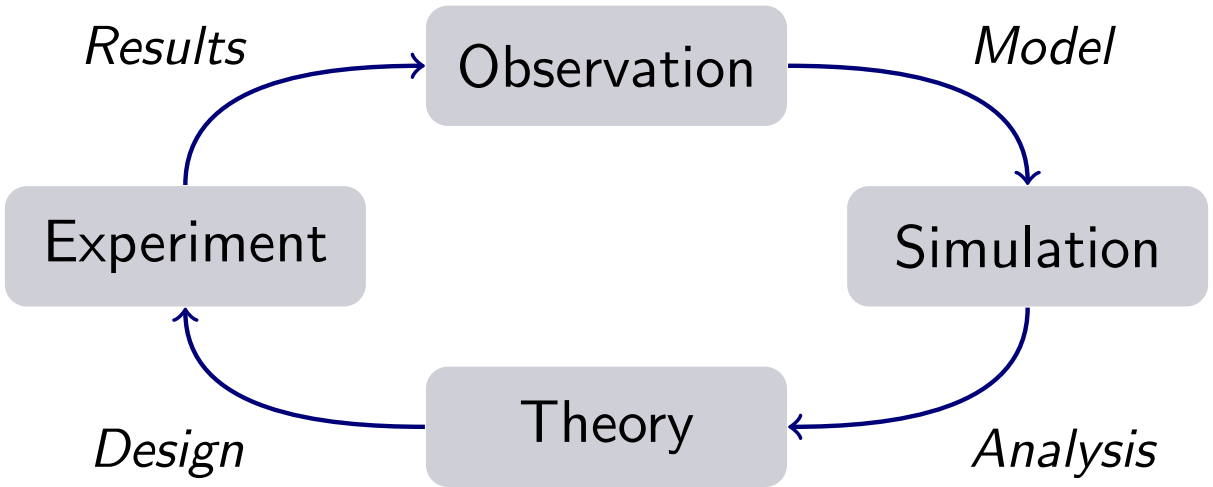
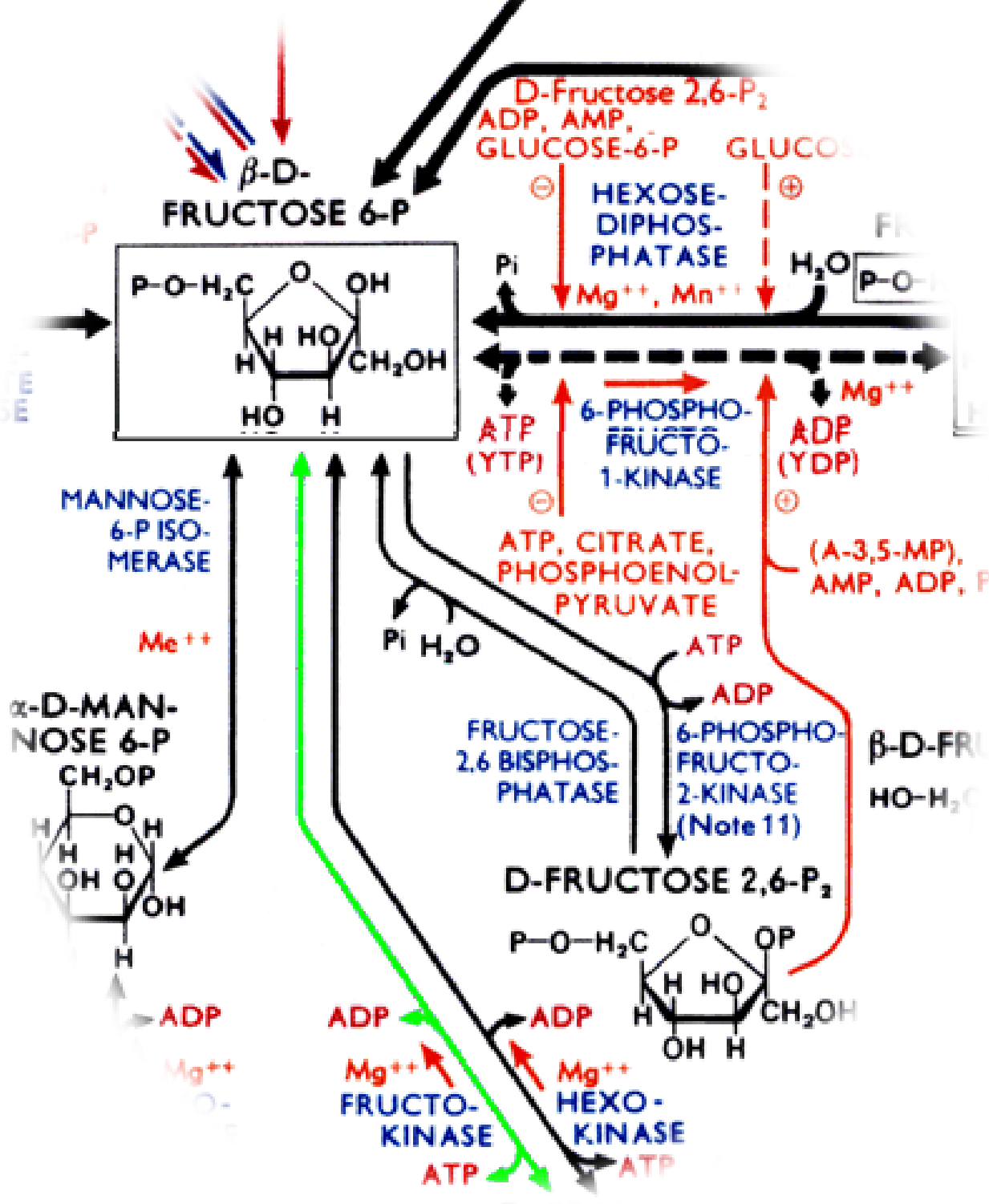
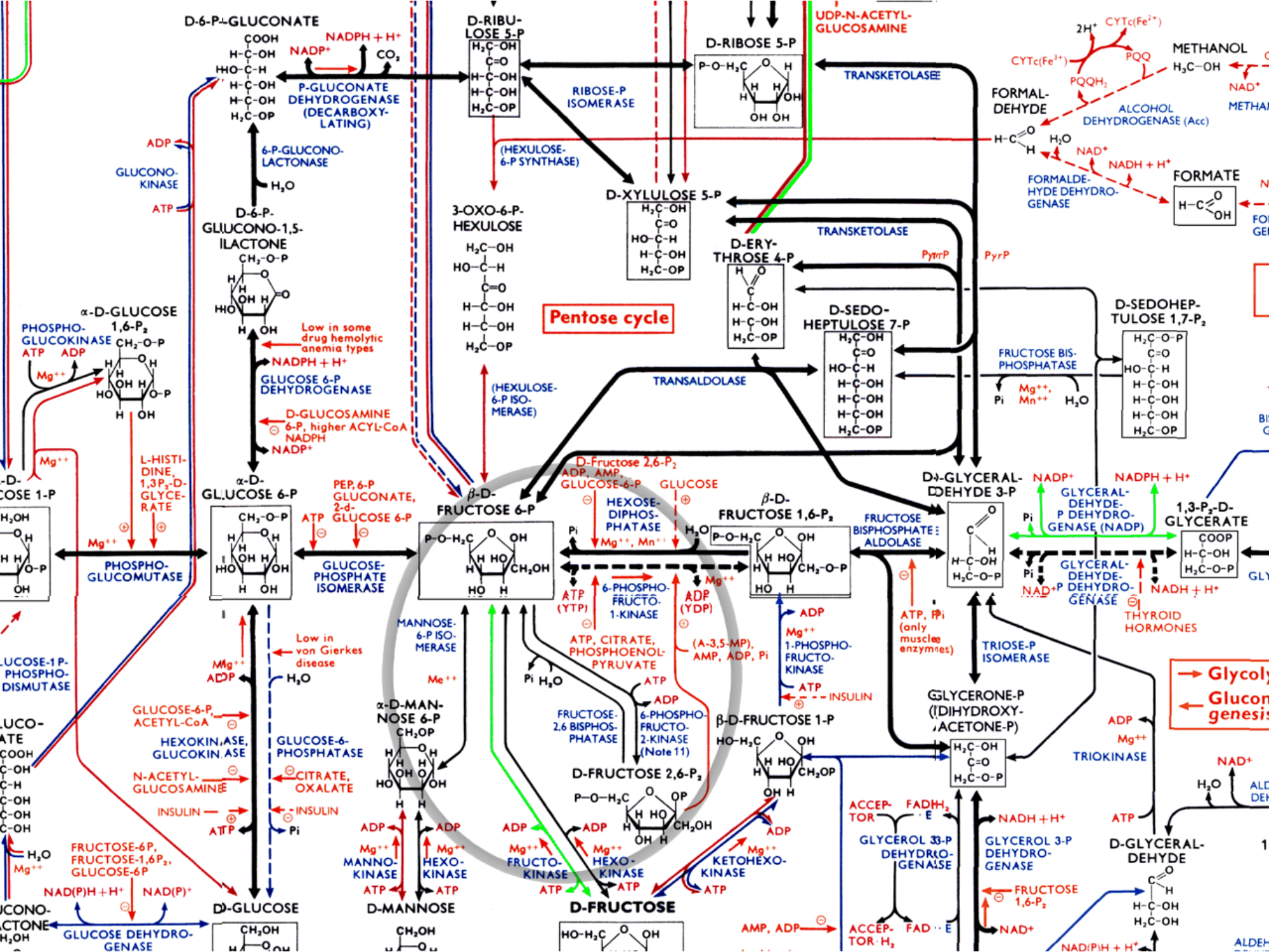
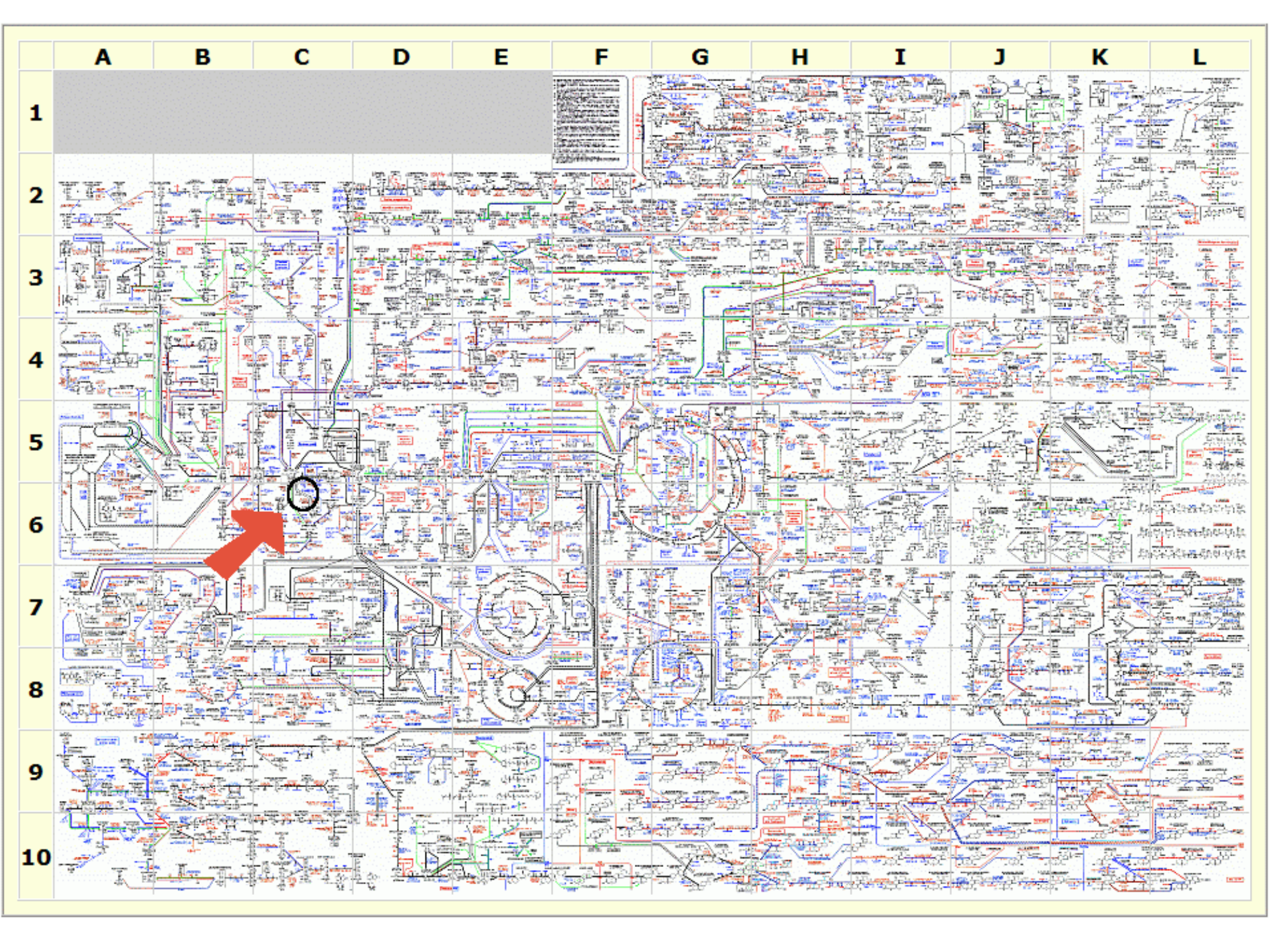



β-D-
FRUCTOSE 6-P
D-Fructose 2,6-P2
ADP, AMP,
GLUCOSE-6-P
HEXOSE-
DIPHOS-
PHATASE
Mg++, Mn++
Pi
H2O
ATP
(YTP)
6-PHOSPHO-
FRUCTO-
1-KINASE
ADP
(YDP)
Mg++
ATP, CITRATE,
PHOSPHOENOL-
PYRUVATE
(A-3,5-MP),
AMP, ADP,
MANNOSE-
6-P ISO-
MERASE
Me++
α-D-MAN-
NOSE 6-P
ATP
ADP
FRUCTOSE-
2,6 BISPHOS-
PHATASE
6-PHOSPHO-
FRUCTO-
2-KINASE
(Note 11)
D-FRUCTOSE 2,6-P2
ADP
Mg++
FRUCTO-
KINASE
ATP
HEXO-
KINASE


D-6-P-GLUCONATE
NADPH + H+
NADP+
CO2
P-GLUCONATE DEHYDROGENASE (DECARBOXY-LATING)
D-RIBU-LOSE 5-P
D-RIBOSE 5-P
UDP-N-ACETYL-GLUCOSAMINE
TRANSKETOLASE
RIBOSE-P ISOMERASE
(HEXULOSE-6-P SYNTHASE)
3-OXO-6-P-HEXULOSE
D-XYLULOSE 5-P
TRANSKETOLASE
D-ERY-THROSE 4-P
PyrP
D-SEDO-HEPTULOSE 7-P
D-SEDOHEP-TULOSE 1,7-P2
FRUCTOSE BIS-PHOSPHATASE
Mg++, Mn++
Pi
H2O
TRANSALDOLASE
(HEXULOSE-6-P ISO-MERASE)
Pentose cycle
6-P-GLUCONO-LACTONASE
H2O
ADP
GLUCONO-KINASE
ATP
D-6-P-GLUCONO-1,5-LACTONE
Low in some drug hemolytic anemia types
NADPH + H+
GLUCOSE 6-P DEHYDROGENASE
D-GLUCOSAMINE 6-P, higher ACYL-CoA
NADPH
NADP+
α-D-GLUCOSE 1,6-P2
PHOSPHO-GLUCOKINASE
ATP
ADP
Mg++
L-HISTI-DINE, 1,3P2-D-GLYCE-RATE
α-D-GLUCOSE 6-P
PEP, 6-P GLUCONATE, 2-d-GLUCOSE 6-P
PHOSPHO-GLUCOMUTASE
GLUCOSE-PHOSPHATE ISOMERASE
β-D-FRUCTOSE 6-P
D-Fructose 2,6-P2
ADP, AMP, GLUCOSE-6-P
GLUCOSE
HEXOSE-DIPHOS-PHATASE
Mg++, Mn++
β-D-FRUCTOSE 1,6-P2
FRUCTOSE BISPHOSPHATE ALDOLASE
D-GLYCERAL-DEHYDE 3-P
NADP+
NADPH + H+
GLYCERAL-DEHYDE-P DEHYDRO-GENASE (NADP)
1,3-P2-D-GLYCERATE
GLYCERAL-DEHYDE-P DEHYDRO-GENASE
NAD+
NADH + H+
THYROID HORMONES
ATP, Pi (only muscle enzymes)
TRIOSE-P ISOMERASE
GLYCERONE-P (DIHYDROXY-ACETONE-P)
6-PHOSPHO-FRUCTO-1-KINASE
ATP (YTP)
ADP (YDP)
ATP, CITRATE, PHOSPHOENOL-PYRUVATE
(A-3,5-MP), AMP, ADP, Pi
1-PHOSPHO-FRUCTO-KINASE
INSULIN
MANNOSE-6-P ISO-MERASE
α-D-MAN-NOSE 6-P
FRUCTOSE-2,6 BISPHOS-PHATASE
6-PHOSPHO-FRUCTO-2-KINASE (Note 11)
β-D-FRUCTOSE 1-P
D-FRUCTOSE 2,6-P2
Low in von Gierkes disease
GLUCOSE-6-P, ACETYL-CoA
HEXOKINASE, GLUCOKINASE
N-ACETYL-GLUCOSAMINE
GLUCOSE-6-PHOSPHATASE
CITRATE, OXALATE
INSULIN
FRUCTOSE-6P, FRUCTOSE-1,6P2, GLUCOSE-6P
NAD(P)H + H+
NAD(P)+
D-GLUCOSE
GLUCOSE DEHYDRO-GENASE
MANNO-KINASE
HEXO-KINASE
D-MANNOSE
FRUCTO-KINASE
HEXO-KINASE
KETOHEXO-KINASE
D-FRUCTOSE
AMP, ADP
ACCEP-TOR H2
FAD
FADH2
E
GLYCEROL 3-P DEHYDRO-GENASE
NADH + H+
FRUCTOSE 1,6-P2
NAD+
TRIOKINASE
D-GLYCERAL-DEHYDE
METHANOL
CYTc(Fe3+)
CYTc(Fe2+)
2H+
PQQ
PQQH2
ALCOHOL DEHYDROGENASE (Acc)
FORMAL-DEHYDE
FORMALDE-HYDE DEHYDRO-GENASE
FORMATE
Glycoly
Glucon genesis


A
B
C
D
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G
H
I
J
K
L
1
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7
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9
10

Scope of Study

Processes

- Metabolic networks
- Regulatory systems: promotion, inhibition
- Signalling pathways
- Gene expression: translation, transcription

Models

- Discrete time, continuous time
- Discrete space, continuous space
- Deterministic, nondeterministic, probabilistic
- Qualitative, quantitative

Topics

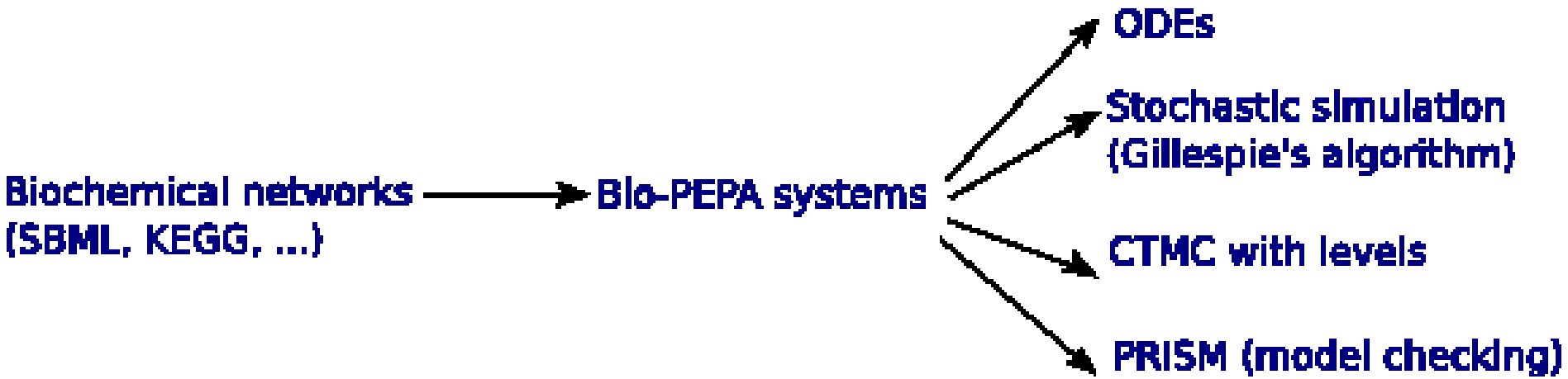
This course explores a variety of mathematical models for biological pathways, and introduces formally precise languages to describe and reason about biological processes.

- Petri Nets: Dynamic system behaviour; analysis of network properties.
- Temporal Logics: Linear time and branching time; model checking.
- Markov Systems: Probabilistic behaviour in continuous time.
- Stochastic Simulation: Gillespie algorithm; reaction kinetics.
- Qualitative vs. Quantitative Analyses: Differential equations.
- Biological Process Algebras: Modularity and compositional reasoning.

Example: Petri Nets

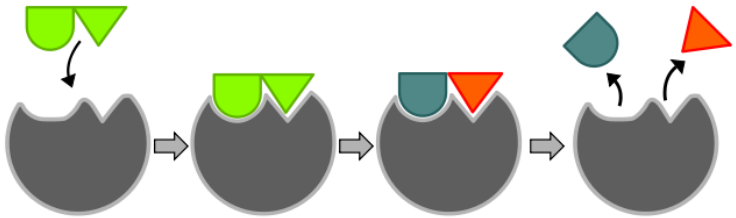
http://genome.ib.sci.yamaguchi-u.ac.jp/~pnp/

Example: BioPEPA



http://biopepa.org/

Example Process: Enzyme Catalysis



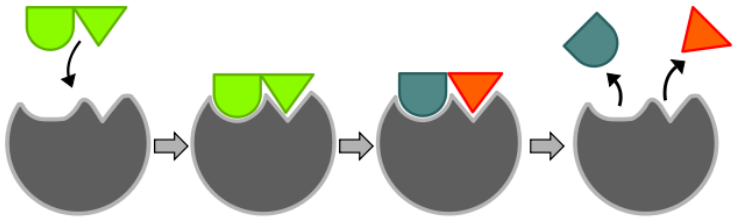
$$S = s(x, y).(x.S + y.(P|P'))$$

$$E = \nu M.e\langle u, r\rangle.t.E$$

$$P = P' = \tau @ k_{degrade}.0$$

$$c_S \cdot S \,\|\, c_E \cdot E$$

Example Process: Enzyme Catalysis



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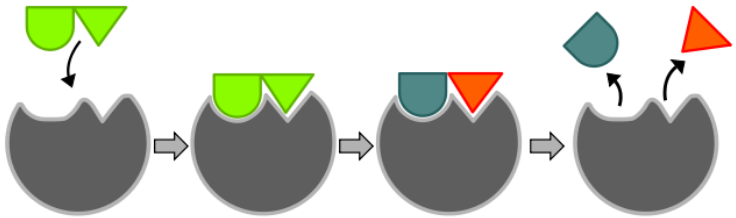
$$c_S \cdot S \,\|\, c_E \cdot E$$

```
enzyme.cpi
...
species E() = {
  site t, u, r;
...
```

Example Process: Enzyme Catalysis



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$$c_S \cdot S \,\|\, c_E \cdot E$$

Cpi tool

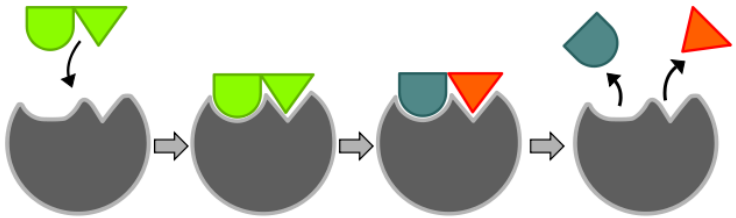
```
enzyme.cpi
...
species E() = {
  site t, u, r;
...
```

ODEs

$$x_2' = -k_1 x_4 x_2 + \ldots$$

$$\vdots$$

Example Process: Enzyme Catalysis



$$S = s(x, y).(x.S + y.(P|P'))$$

$$E = \nu M.e\langle u, r\rangle.t.E$$

$$P = P' = \tau@k_{degrade}.0$$

$$c_S \cdot S \,\|\, c_E \cdot E$$

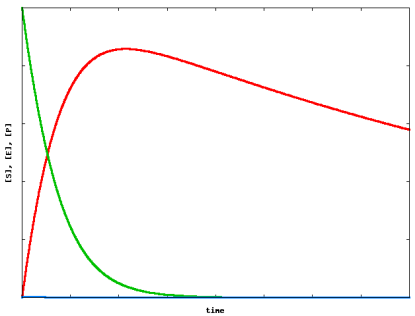
Cpi tool *Octave*

```
enzyme.cpi
...
species E() = {
  site t, u, r;
...
```

ODEs

$$x_2' = -k_1 x_4 x_2 + \ldots$$

$$\vdots$$



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